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Amendment and Response

Serial No.: 10/718,359

Confirmation No.: 3660

Filed: November 20, 2003

For: NaCT AS A TARGET FOR LIFESPAN EXPANSION AND WEIGHT REDUCTION

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-11. (Cancel)

12. (Previously Presented) An isolated polypeptide, wherein the polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the polypeptide is capable of Na⁺-dependent transmembrane transport of citrate.

13. (Previously Presented) The isolated polypeptide of claim 12, wherein the polypeptide comprises SEQ ID NO:6.

14-19. (Cancel)

20. (Currently Amended) An isolated polypeptide comprising an amino acid sequence having at least 75% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na⁺-dependent transmembrane transport of citrate.

21. (Currently Amended/Withdrawn) The isolated ~~polynucleotide~~ polypeptide of claim 20, wherein the encoded Na⁺-dependent transmembrane transport of citrate is modulated by Li⁺.

22-26. (Cancel)

27. (Previously Presented) The isolated polypeptide of claim 20, wherein the polypeptide capable of Na⁺-dependent transmembrane transport of citrate requires multiple Na⁺ ions for transport coupling.

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28. (Previously Presented) The isolated polypeptide of claim 20, wherein the transmembrane transport of citrate is electrogenic.

29-35. (Cancel)

36. (Previously Presented) The isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 80% identity to SEQ ID NO:6.

37-44. (Cancel)

45. (Previously Presented) The isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 85% identity to SEQ ID NO:6.

46. (Cancel)

47. (Previously Presented) The isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 90% identity to SEQ ID NO:6.

48. (Cancel)

49. (Previously Presented) The isolated polypeptide, of claim 20, the polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide demonstrates transmembrane transport of citrate.

50. (Previously Presented) The isolated polypeptide of claim 20, the polypeptide comprising an amino acid sequence having at least 99% identity to SEQ ID NO:6.

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51-56. (Cancel)

57. (Withdrawn) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

- contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 with an agent;
- measuring citrate transport into the host cell in the presence of agent;
- and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;
- wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;
- wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

58. (Withdrawn) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

- contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 with an agent;
- measuring citrate transport into the host cell in the presence of agent;
- and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;
- wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;
- wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

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59. (Withdrawn) A method of identifying an agent that modifies transmembrane citrate transporter activity comprising:

contacting a host cell expressing a transmembrane citrate transporter polypeptide of claim 12 with an agent wherein the encoded Na^+ -dependent transmembrane transport of citrate is stimulated by Li^+ ;

measuring citrate transport into the host cell in the presence of agent;

and comparing citrate transport into the host cell in the presence of the agent to citrate transport into the host cell in the absence of the agent;

wherein a decreased transport of citrate into the host cell in the presence of the agent indicates the agent is an inhibitor of transmembrane citrate transporter activity;

wherein an increased transport of citrate into the host cell in the presence of the agent indicates the agent is a stimulator of transmembrane citrate transporter activity.

60-75. (Cancel)

76. (Withdrawn) A method of identifying an agent that modifies Na^+ -dependent transmembrane citrate transporter activity comprising:

contacting a host cell expressing a Na^+ -dependent transmembrane citrate transporter of claim 12 with an agent;

measuring the citrate-induced inward electrical current into the host cell in the presence of agent; and

comparing the citrate-induced inward electrical current into the host cell in the presence of the agent to the citrate-induced inward electrical current into the host cell in the absence of the agent;

wherein a decrease in the inward electrical current into the host cell in the presence of the agent indicates the agent is a blocker of Na^+ -dependent transmembrane citrate transporter activity;

wherein an increase in the inward electrical current into the host cell in the presence of

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the agent indicates the agent is a stimulator of Na^+ -dependent transmembrane citrate transporter activity.

77. (Withdrawn) A method of identifying an agent that serves as a substrate of a Na^+ -dependent transmembrane citrate transporter comprising:

contacting a host cell expressing a Na^+ -dependent transmembrane citrate transporter of claim 12 with an agent; and

determining the entry of the agent into the cell via the Na^+ -dependent transmembrane citrate transporter in the presence of agent;

wherein entry of the agent via the Na^+ -dependent transmembrane citrate transporter indicates the agent is a substrate of a Na^+ -dependent transmembrane citrate transporter.

78. (Previously Presented) A recombinant polypeptide, wherein the recombinant polypeptide is encoded by a polynucleotide that hybridizes to SEQ ID NO:5 under stringent hybridization conditions, wherein the recombinant polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

79. (Previously Presented) The recombinant polypeptide of claim 78, wherein the recombinant polypeptide comprises SEQ ID NO:6.

80. (Previously Presented) A recombinant polypeptide comprising an amino acid sequence having at least 75% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na^+ -dependent transmembrane transport of citrate.

81. (Previously Presented) The recombinant polypeptide of claim 80, wherein the encoded Na^+ -dependent transmembrane transport of citrate is modulated by Li^+ .

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82. (Previously Presented) A recombinant polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:6, wherein the polypeptide is capable of Na⁺-dependent transmembrane transport of citrate.

83. (Previously Presented) The recombinant polypeptide of claim 82, wherein the Na⁺-dependent transmembrane transport of citrate is modulated by Li⁺.